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1: The Amino Acid Sequence of Apo B-100

10	20	30	40	50	60	70	80	90	
EEEMLENSLVCPKD	ATRFKHLRKYTYN	YEAESSGVPGTAD	RSATRINCKVELE	VPQLCSFILKTSQ	CTLKEVYGFNPEG	KALLKTKNSEEFA	AAMS	100	
RYELKLAIEGKQV	FLYPEKDEPTYIL	NIKRGIIISALLV	PPETEEAKQVLF	LDTVYGNCSHTF	TVTKRGNVATEI	STERDLGQDRFK	PVRTGISPLAL	200	
IKGMRPLSTLIS	SSQSCQYTLDAK	RKHVAEAIKEQHL	FLPFSYNNKYGM	VAQVTQTLKLED	TPKINSRFFGEG	TCKMGLAFESTK	STSPPKQAEAVLK	300	
TLQELKLTISEQ	NIQRANLFNKL	VTELRGLSDEAV	TSLPQLIEVSPIT	LQALVQCGQPQC	STHILQWLKRVH	ANPLLIDVVTYL	VALIPEPSAQQLR	400	
EIFNMARDQRS	RATLYALSHAVN	NYHKTNPTGTQ	ELLDIANYLMEQ	IQQDDCTGDEDY	TYLILRVIGNMG	QTMEQLPELKSS	ILKCVQSTKPSLMIQKAA	500	
IQALRKMEPKD	KQDEVLLQTFL	DDASPGDKRLA	AYMLMRSPSQAD	INKIVQILPWEQ	NEQVKNFVASHI	ANILNSEELD	IQDLKKLVKEALKESQLPTV	600	
MDFRKFSRNYQ	LKSVSLPSLDP	ASAKIEGNLIFD	PNNVLPKESML	KTTLTAFGFA	SADLIEIGLEGK	GFEPTEALFGK	QGFPPDSVNKALYWNVNGQVP	700	
DGVSKVLVDH	FGYTKDDKHEQ	DMVNGIMLSVE	KLKDLKSKEVP	PEARAYLRILGE	ELGFASLHDLQ	LLGKLLMGART	LQIPQMIGEVIRKGSKNDFFL	800	
HYIFMENAFEL	PTGAGLQLQIS	SGVIAPGAKAG	IKLEIVANMQAEL	VAKPSVSVEFV	TNMGIIIPDFAR	SGVQMNTNFFH	ESGLEAHVALKAGKLKFIIP	900	
SPKRPVKLLSG	NTLHLVSTTKTE	VIPPLIENRQSW	SVCKQVFPGLNY	CTSGAYSNASST	DSASYPLTGDTR	LELELRPTGEI	EQYSVSATYELQREDR	1000	
ALVDTLKFTQAE	GAKQTEATMTFK	YNRQSMTSSSEV	QIPDFDVLGTIL	RVNDESTEGKTS	YRLTLDIQNKKI	TEVALMGHLSCD	TKEERKIKGVISIP	1100	
RLQAEARSEILA	HWSPAKLLQMD	SATAYGSTVSKR	VAWHYDEEKIEF	EWNTGTNVDTK	MTSNFPVDLSDY	PKSLHMYANRLD	HRVPETDMTFRHVG	1200	
SKLIVAMSSWLQ	KASGSLPYTQT	LQDHLNSLKEFN	LQNMGLPDFHIP	ENFLKSDGRVKY	TLNKNSLKIEIPL	PFGKSSRDLKML	ETVRTPALHFKSVG	1300	
FHLPSREFQVPT	FTIPKLYQLQV	PLLGVLDLSTN	VYSNLYNWASYS	GGNTSTDHFSLR	ARYHMKADSVVD	LLSYNVQSGETT	YDHKNTFTLSCDGLR	1400	
HKFLDSNIKFSH	VEKLGNNPVSK	GLLIFDASSWG	PQMSA\$VHLDS	KKQHLFVKEVK	IDGQFRVSSFYAK	GTYGLSCQRPNT	GRLNGESNLRFNSSYL	1500	
QGTNQITGRYED	GTLSLTSTSD	LQSGIKNNTAS	LKYENVELTLK	SDTNKGKYNFATS	NKMDMTFSQNALL	RSEYQADYESL	RFFSLLSGSLNSHGLELN	1600	
ADILGTDKINS	GAHKATLRIGQ	DGISTATTNLK	CSSLVLENELNA	ELGLSGASMKL	TTNGRFRHNAK	FSLDGKAALTE	LSGLSAYQAMILGVDSKNIF	1700	
NFKVSQEGKL	SNDMMGSAEMK	FDHTNSLNIAG	LSLDFSSKLDNI	YSSDKFYKQTV	NLQLQPYSLVTT	LNSDLKYNALD	LTNNGKLREPLKLVAGNL	1800	
KGAYQNNEIKH	IYAISSAALS	ASYKADTVAKVQ	GVFEFSHRLNTD	IAGLASAIDMST	NYNSDSLHFSNV	FRSVMAPFTMT	IDAHTNGNGLALWGEHTGQL	1900	
YSKFLKAEPLA	FTFSDYKGST	SHHLVSRKSI	SAALEHKVSALL	TPAEQTGTWKL	KTOFNNEYSQD	LDAYNTKDKIG	VELTGRTLADLTLLDSP	2000	

FIG. 1

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10	20	30	40	50	60	70	80	90																		
LLLSEPINI	DAVEK	PQEF	IVAF	VKYD	NQDV	HSIN	LPFF	ETLQ	EYFERN	RQTI	IIVV	VENV	QRNL	KHIN	IDQF	VRKY	RAAL	GKLP	QQAND	YLN	2100					
SFNWERQ	SHAKE	L	TAL	TKKYR	ITEND	IQIAL	DDAK	INFNE	KLSQL	QTYMI	QDQY	IKOSY	DLHDL	KIAIANI	IDEI	IEKLS	DEHYH	JRVNL	VKTIH		2200					
DLHLFI	ENIDFN	KSGS	TASW	IQNV	DTKYQ	IRIQ	IEKL	QOLKR	HQNI	IDIQ	HLAG	KQHIE	ADRV	LLDQL	GTTIS	FERIN	DVLE	HVKHF	VINL	IGD	2300					
FEVAEK	INAFRA	KVHEL	IERVE	VDQIQ	VLMD	KLVEL	THQY	KLKET	IQKLS	NVLQQ	WKIDY	FEKL	VGFID	DAVK	KLNEL	SFKTF	IEDV	NKFL	DMLIK	KL	2400					
KSFYHQ	FVDE	TNDK	IREV	TQRL	NGEI	QALE	LPQK	AEAL	KLFL	EETK	ATVAV	LESL	QTKIT	LIIN	WLQE	ALSS	ASLA	HMAK	AKFRE	TLED	TRDR	MYDM	2500			
IQQELQ	RYLS	VGQV	YSTL	VTYIS	DMW	TAAK	NLTD	FAEQ	YSIQ	DWAK	RMKAL	VEQ	FTVPE	IKIT	ILGT	MPAF	EVSL	QALQ	KATF	QTPD	FIVPL	TDLR	IP	2600		
SVQINF	KDLK	NIKIP	SFST	PEFT	ILNT	FHIP	SFTI	DFVEM	KVKI	IRTI	DQM	NSLQ	WPVP	DIYLR	DLK	VEDI	PLAR	ITL	PDFR	LP	EIAI	PEFI	IP	TLN	2700	
LNDFQV	PD	HIPE	Q	PHIS	HTIE	VP	TGKL	YSIL	KIQS	PLFT	DAN	ADIG	NGTTS	ANEAG	IAAS	ITAK	GESK	LEVLF	NDFQ	ANAQ	LSNP	KINP	LAL	KES	2800	
VKFSSK	YLRT	EHGSE	MLFF	GNAI	E	GKSNT	VASL	HTEK	N	TELS	NGV	IVK	INNQL	TLDS	NTKY	FHKL	NI	PKL	DFSS	QADL	RNEIK	TLLK	AGHIA	WTSS	GKG	2900
SWKWA	CP	FSDE	G	THES	QIS	FTIE	GP	TSF	GLSN	KINS	KHLR	VNQNL	VYES	GS	NFSK	LEIQ	SQVDS	QHVH	SVLTAK	G	MA	LFG	EGKAE	FTGR	HDAHLNG	3000

10	20	30	40	50	60	70	80	90																														
KVIGTL	KNSL	FFSA	Q	FEIT	ASTN	NEG	NLKV	RFLRL	TGKI	DFL	NNYAL	FLSP	AAQAS	QVSAR	FNQY	KYNQ	NFSAG	NNEN	IMEA	HV	GIN	GEAN	LDFLN	3100														
IPLTI	PEMR	LPY	TIIT	TPPL	KD	FLS	WEK	TGLKE	FLK	TTKQ	SFDL	SVKA	QYK	KNK	HRHS	ITN	PLAVL	CEFI	SQIS	KSF	DRH	FEK	NRNN	VALDF	VTKSY	NETK	3200											
IKFDKY	KAES	HDEL	PR	TFQIP	GYTP	VVN	VEV	SPFT	IE	MSAF	GYW	FPK	AV	MP	SFSIL	GSD	VRV	PSYTL	ILP	SLEL	PVLH	VPR	NLKL	SLP	HFKE	LCTIS	3300											
HIFIP	AMGN	ITYD	FSK	SSVIT	LTNA	ELFN	QSDI	VAHL	SSSS	VIDAL	QYK	LEG	TTRL	TRK	RGLK	ATAL	SLSN	KFVE	GSHN	STVSL	TTKN	MEV	SVAK				3400											
TTKAE	IPIL	RMNF	KQEL	NGNT	KS	KPTV	SSS	MEFKY	DFN	SSML	YSTA	KG	AVD	HKLS	ESL	TSYF	SIES	STK	GDV	KGSV	LSRE	YS	SGT	IA	SEAN	TYL	NSKSTR	3500										
SSVKL	QGT	SKIDD	IN	WLE	VKEN	FAGE	ATLQ	RIY	SLWE	HSTKN	HLQ	LEGL	FFT	NGE	HTSK	ATLE	SPWQ	MSAL	VQVH	ASQ	PSS	HF	DFD	PD	LQ	GE	VALNANTK	3600										
NQKIR	WKN	EVRI	THSG	SFQ	SQV	EL	SN	DQ	EKA	HL	D	IAG	S	LEG	HLR	FLK	NIIL	PVYD	KSL	WD	FLK	LD	VTT	SIG	RRQ	HLRV	STAF	VVYTK	NPNG	VSFS	IPV	KVLA	3700					
DKFIT	PGL	K	NDL	NSVL	VMPT	F	HP	FTDL	QV	PSCK	LDFR	EIQY	KKL	RTSS	FALN	PTL	PEV	K	FPE	VDVL	TKY	SQ	PED	SLIP	FFE	ITV	PES	QLTV	SQFTL				3800					
PKSVS	DGIA	ALDL	NAV	ANK	AD	FEL	PTI	I	VPEQ	TEI	PSIK	FSV	PAGI	VIPS	FQAL	TAR	FEV	DSP	VYNAT	MS	ASL	KNK	ADY	VE	TVL	D	SCS	STVQ	FLEYE				3900					
LNVLG	THK	I	EDG	T	LASK	T	KG	T	LA	HR	D	FSAE	Y	EED	GK	F	EGLQ	E	WEG	K	AHLN	IK	SPA	FTDL	HLR	YQ	KDK	KGIS	TSA	ASP	AVGT	V	GMD	DEDD	DDFSK	MNF	YYS	4000

FIG. 1 Cont.

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10	20	30	40	50	60	70	80	90	
PQSSPDKLTIFKTELVRRESDEETQIKVNWEEEAASGLTSLKDNVPKATGVLVDYVYNKYHWEHTGLTREVSSKLRRNLQNNAEWVYQGAIRQIDDID	4100								
VRFQKAASGTTGTYQEWKDKAQNLYQELLTQEGQASFOGLKDNVFDGLVRVTQKFHMKVKHLIDSLIDFLNFPFQFPGKPGIYTREELCTMFIREVGTV	4200								
LSQVYSKVHNGSEILFSYFQDLVITLPPFELRKHLIDVISMYRELLKDLSCAEQEVFKAIQSLKTTEVLRNLDLLQFIFQLIEDNIKQLKEMKFTYLIN	4300								
YIQDEINTIFNDYIPYVFKLLKENLCLNLHKFNEFIQNELQEQASQELQQIHQYIMALREEYFDPISIVGWTVKYYELEEKIVSLIKNLLVALKDFHSEYIV	4400								
SASNFTSQLSSQVEQFLHRNIQEYLSILTDPDGKGKKEIAELSATAQEIIKSQAIAATKKIISDYHQQFRYKLDQFSDQLSDYYEKFIAESKRLIDLISQN	4500								
YHTFLIYITELLKKLQSTTVMPYMKLAPGELTIIL									

FIG. 1 Cont.

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Comparison of SH3-like Regions in Apo B-100 to Known SH3 Domains of Signal Transduction Proteins. Percent similarities are indicated at Right margin.

		10	20	30	40	50	60	
B1	KYTYNVEA--ESSGVPGTADSR-SATRINCKVELEVPQLCSFILKTSQ							
R9	AYDFNYPIKKDSSQLL-SVQQGETIYILN-KNSSGWDG--LVIDDSN							
	Y**NY * *SSS ** *** ** *N K *** S*							55%
B2	VYGFNPEGKALLKTKNSEFAAAMSRVELKLAIPGKQV--FLYPE							
R33	LYDFVASGDNLTSLITKGEKRLVLGYNHYNGEWCEAQTNGQGNVPSN							
	*Y F * G L TK ***** *Y* * ** K* *** *							51%
B3-1	FLPFSYNKYGMVAQVTQTLKLEDTPKINSRFF-GE-GTKKMGLAF							
R35	LFDYKAQREDELT--FTKSAIQNVEKQEGGWWRGDYGGKKQ-LWF							
	** * ** * *T ** *** K * ** G* G KK L*F							54%
B3-2	FLPFSYNN-KYG-MVAQVTQTLKLEDTPKINSRFF-GEGTKKM---GLA-FE							
R18	LH--SYEPSHDGDLGFEKGEQLRILEQSGE----WwKAQ-SLTGQEGFIPFN							
	* SY* * G ***** * L** E** ** ** * G** F*							51%

FIG. 2A

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Comparison of SH3-like Regions in Apo B-100 to Known SH3 Domains of Signal Transduction Proteins. Percent similarities are indicated at Right margin.

B4	YTYLILRVIGNMQTMEQLTPEL-KSSILKCVQSTKPSLMIQAAIQALRKMEPKDKD---QEVLL	
R52	VVALFD-YAA-VNDR-DL--QVLKGE--K-LQVLRSTG--DWMRLARSLVTG--REGVYPSNFFVAP	50%
	* *L* *** * * *L ** K K *Q * * ***** *L ** **V**	
B5	AFGFASADLIEIGLEGKGFEPTLEALFGKQGFPPDS-VN--KALYWNQGVQVPD	
R34	LYDFAAENPDELTFNEGAVVTVINKSNP-D-WM-EGELNGQRGVFPAS--YVE	59%
	FA* ** E* ** ** ** * ** * *N ** ***	
B8	FGYTKDOKHEQ-DMVNGIMLSVEK--LIKDLKSK--EV-PEARAYLRILGEE	
R25	YDYKKEE--EDIDLHLGDILTVNKGSLVALGFSGQEAKEPTEEIGWLNQY-NE	56%
	* Y K** E* D* G ***V*K L** S E* PE **L * *E	
B8	FDYHQFVDETNDK-IREVTQRLNGEIQ-ALELPQKAEALKLFLEETKAT-V-AVYL	
R32	YDY-----QEKSPREVTMKK-GDILTLLNSTNK-DWMKVEVND-RQGFVPAAYV	52%
	*DY **K *REV* * G*I *L* *K ***K* *** * V A*Y*	

FIG. 2B

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B9-1	YDM--DIQELQRYLSLVGQVYSTLVITYISDWWT--LAAK-NLTDFAEQYSIQDWA	
R35-2	FDYKAQREDELTFTKSAIIQNVEKQDGG---WWRGDYGGKKQLW-FPSNY-VEEMI	
	*** * **EL S** Q * WW ***K *L F* *Y *****	54%
B9-2	YDMDIQ----QELQRYLSLVGQVYSTLVITYISDWWTLAAKNLTDFAEQ-YSIQDWAKRMK	
R43	IQ-DYEPRLTDEI-RI-SL-GEKVK-ILATHDGNCLVEKCNTRKGTIHVSVD--KRYL	
	*Q D** *E* R* SL G* * *** *D W L* K T * *S**D KR*	57%
B9-1	YQMDI--QQELQ--RYLSLVGQVYSTLVITYIS-DWW---TLAA-KNLTDFAEQYSIQDWA	
R49	YDYEARTEDDLTFTK-----GEKF-HILNTEGDWWEARSLSSGK--T--G-CIPSNYVA	
	Y**** ***L * G* * ** DWW *L** K T * * * *A	51%
B10	TYDFSFK---SS-VITLNTNAE-LFNQSDIVAHLLSSSSVIDALQY-----KLE	
R9-2	DFNYPICKDSSQLLSVQ-QGETIY-----ILNK--NSS-GWWDGLVIDDSNGKVN	
	DF ** K SS ***** **E ** I* * SS **D*L * K**	56%
B11	KYDFNSSMLYSTAKGAVDHKLSLESLTS-----YFSIESSTKGDVKGSVLSREY	
R47	EPYVAIK-AYTAVEGDEVSLLEGEAVEVIHKLLDGMWVIR---KDDVTGYFPSMYL	
	* * *Y*** G L E** ** I K DV G **S *	50%

FIG. 2C

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Comparison of SH3-like Regions in Apo B-100 to Known SH3 Domains of Signal Transduction Proteins. Percent similarities are indicated at Right margin.

B12	LWDFLKLD-----VTTSIGRRQHLRVSTA-----FVYTKNPNGYSFIPVKVLADKFITPGLKL	54%
R3	LYDF-KAEKADELTTYVG--ENL-FICAHHNCEWFIK-PIGRLGPGGL-VPVG-FVSI-IDI	
	L*DF K** *TT *G * L * A ****K P G * * V** F*** * *	
B13	VLYDYVVKY-HWEHTGLT-LR-EVSSK-LRRNLQNNAEWYQGAIRQIDDI	
R3-2	VLYDF--KAEKADE--LTTYVGENLFICAHHN-----CEWFI---AKPIGRL	
	VLYD* K* *** LT * E ***N EW** ** I *	51%
B14	KPGIY--TREEELCTMFIREVGTVL-----SQVYSKVHNGSE--ILF-SYFQ--DL	
R36	LFGFVPETKEELQ-VMPGNIVFVLKKGNDNWATVM--F-NG-QKGLVPCNYLEPVEL	
	G* *T*EEL * ** VL * V* * NG * *** *Y** *L	56%
B15	GKPGIYTREELCTMFIREVGTVLSQ-----VYSKVHNGS-E---ILFS-YFQ--D	
R59	AKFDYVAQQEQE LDIKKNERLLDDSKSWM-RVRN-SMNKTGFVPSNYVERKN	
	K *** *E * I* ** ** *V*N S * ***S Y** *	53%

FIG. 2D

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Identification of the regions of apo B-100 and the proteins compared in Figures 2A-2D.

<u>Reference Protein Name:</u>	<u>SEQ ID NO.</u>
Apo B-100 region B1 (aa 24-69)	SEQ ID NO:3
r9 (aa 66-114). cell division control protein 25 gim 4857	SEQ ID NO:4
Apo B-100 region B2 (aa 75-119)	SEQ ID NO:5
r33 (aa 69-114). Abl proto-oncogene tyrosine kinase (P150) gim 13887	SEQ ID NO:6
Apo B-100 region B3-1 (aa 240-283)	SEQ ID NO:7
r35 (aa 799-841). 1-Phosphatidylinositol-4,5-bisphosphate phosphodiesterase gamma (PLC-gamma. PLC-II) gim 18895	SEQ ID NO:8
Apo B-100 region B3-2 (aa 240-284)	SEQ ID NO:9
r18 (aa 69-114). Lck proto-oncogene tyrosine kinase (P56-LCK) gim 14213	SEQ ID NO:10

FIG. 2E

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IDENTIFICATION OF THE REGIONS OF APO B-100 AND THE PROTEINS
 COMPARED IN FIGURES 2A-2D

Apo B-100 region B4 (aa 457-518)	SEQ ID NO:11
r52 (aa 57-109). BLK protein tyrosine kinase (B lymphocyte kinase) (P55-BLK) gim 13991.	SEQ ID NO:12
Apo B-100 region B5 (aa 652-700)	SEQ ID NO:13
r34 (aa 984-1031). Myosin IC heavy chain gim 16466	SEQ ID NO:14
Apo B-100 region B6 (aa 711-756)	SEQ ID NO:15
r25 (aa 12-61). Phosphatidylinositol 3-OH gim 18072	SEQ ID NO:16
Apo B-100 region B8 (aa 2403-2454)	SEQ ID NO:17
r32 (aa 976-1021). Spectrin alpha chain, brain gim 23407	SEQ ID NO:18
Apo B-100 region B9-1 (aa 2497-2547)	SEQ ID NO:19
r35-2 (aa 800-850). 1-Phosphatidylinositol-4, 5-bisphosphate phosphodiesterase gamma. (PLC-gamma, PLC-II) gim 18895	SEQ ID NO:20
Apo B-100 region B9-2 (aa 2497-2551)	SEQ ID NO:21
r43 (aa 444-496). Nuclear fusion protein FUS1 gim 9498	SEQ ID NO:22
r49 (86-134). Fgr Proto-oncogene Tyrosine gim 14097	SEQ ID NO:23
Apo B-100 region B10 (aa 3311-3355)	SEQ ID NO:24
r9-2 (aa 66-114). Cell division control protein 25 gim 4857	SEQ ID NO:25
Apo B-100 region B11 (aa 3434-3482)	SEQ ID NO:26
r47 (aa 229-280). Neutrophil Cytosol Factor 1 (NCF-47K) gim 16659	SEQ ID NO:27
Apo B-100 region B12 (aa 3657-3710)	SEQ ID NO:28
R3 (aa 162-201)Bem-1 protein gim 3905	SEQ ID NO:29

FIG. 2F

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IDENTIFICATION OF THE REGIONS OF APO B-100 AND THE PROTEINS
COMPARED IN FIGURES 2A-2D

Apo B-100 region B13 (aa 4053-4099)	SEQ ID NO:30
r3-2 (aa 163-214)Bem-1 protein gim 3905	SEQ ID NO:31
Apo B-100 region B14 (aa 4180-4222)	SEQ ID NO:32
r36 (a 248-299). Neutrophil NADPH oxidase factor (P67-PHOX) gim 16660	SEQ ID NO:33
Apo B-100 region B15 (aa 4179-422)	SEQ ID NO:34
r59. Cytoplasmic protein gim 16669	SEQ ID NO:35

FIG. 2G

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Comparison of SH2-like Regions in Apo B-100 to Known SH2 Domains of Sign Transduction Proteins.

9.	WYHASLTRAQAEHMLMRV-----PRDGA-FLVRKRNEPNSYAISFR-AEGKIKH	
10.	FFGEG-TK-----KMGLAFESTKSTSPPKQ-AEAVLKTQLQELKKLTISEQNIQ-RANL	
	** T* *M* * P** A **** *E* ***S **	
9.	C-RVQQEGTVMLGNSEFDSLVDLISYYEKHPL-----YRKMCLK	
10.	FNKLVTELRGLSDEAVT-SLLPQLIEVSSPITLQALVQCGQPCSTHLOWLKRVDHAN	40%
	** E * ** SL* *LI* L *****	
5.	WFHG--KISKQAEAYNLLMTVGQACSFVLRPS-DNTPGDY-SLYFRTSENIRFKICP	
11.	IMLSVEKLKDLKSKE---VPEAR-AYLRILGEEL-G-FASLHDLQLLGKLLMGAR	
	** K* K* V *A ***R* ** G * SL *	
5.	T-----PNNQFMGGRYN-SSIGDIDHYRK-EQIVEGYY--LKEP	
11.	TLQGIQQ---MIGE-VIRKGSKNDFFLHYIFMENAFELPTGAGLQL	42%
	T P* M*G ** S D** HY E***E * **	

FIG. 3A

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Comparison of SH2-like Regions in Apo B-100 to Known SH2 Domains of Sign Transduction Proteins.

5. WFHGIS--KQEAYNLMTVGACSFLVRPSDNTPGDYSLFRTSENIQ-----R--F
16. YFH-KLNIPK---LD--FSS-QAD---LR--NEIK---TLL-KAGHIAWTSSGKGSW
 FH K K ** ** QA *R ** *L* ** * * *
5. KI-CPTPNNQFMMGRYNSSIGDIIDHRKEQIVEGYYLK
16. KWACPRFSDE---GTH--ESQISFTIEGPLTSFGLSNKINS
K* CP * ** G * *S I I* * * *
6. WYWGDISR---EEVNE---KLROTPDGTFLVRDASSKIQG--DYTLTRKGGNNKL
17. FFSAQPFEITASTNEGNLKVR-----FPLR-LTGKIDFLNNYALFLSPSAQQAS
 ** *** NE K*R F**R ** KI* *Y*L L ***
6. IKVFHR--DGKYG--FSEPLTFCSVDLITHRHESLAQYNAKLDTRLLYPVSKY
17. WQVSARFNQYKYNQNFSAGNNEN-IMEA--HVGINGEANLDF-LNIPLTIPEMRL
 * V R * KY FS **E* H* * A**** L** L *P **

41%

55%

FIG. 3B

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Comparison of SH2-like Regions in Apo B-100 to Known SH2 Domains of Sign Transduction Proteins.

8.	WFHGKLGAG-RDGRHIAERLLTEYCETGAPDGSFLVRESETFVGD-YTL ^u SFWRNGK	
21.	FP-GKPGIYTR ^u E-----ELC-----TMFIREVGT ^u LSQVYSK--VHNGS	
	** GK*G* R* E*C *****RE T** * Y* **NG	
8.	VQHCRIHSRQDAGTPKFFLTDNL-VFD--SLY-DLITH-----YQQVPLRCNEFEMRLSE	
21.	-EILFSYF-QDLVITL ^u PFELRKHK ^u LIDVISMYRELL-K ^u LSKEAQEV-FKAIQS-LKTTE	34%
	* QD* *F **D S*Y *L* * Q*V ** * ** *E	

Structurally important motifs are indicated by double underline. Percent similarity is :
 right.

FIG. 3B Cont.

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Identification of the reference proteins as well as the apoB-100 regions used in the above alignments

<u>Reference Protein Name:</u>	<u>Sequence ID No.</u>
9. = phospholipase Cyl. Residues 668-753	SEQ ID NO:36
10. = Apo B-100 region 10. aa(271-377)	SEQ ID NO:37
5. = GTPASE-activating protein (GAP) (RAS P21 PROTEIN ACTIVATOR). Residues 348-437	SEQ ID NO:38
11. = Apo B-100 region 11. aa(727-819)	SEQ ID NO:39
5. GTPASE-activating protein (GAP) (RAS P21 PROTEIN ACTIVATOR). Residues 348-435	SEQ ID NO:40
16. = Apo B-100 region 16. aa(2861-2938)	SEQ ID NO:41
6. = p85 α . Residues 326-424	SEQ ID NO:42
17. = Apo B-100 region 17. aa(3011-3110)	SEQ ID NO:43
8. = phospholipase Cyl. Residues 550-655	SEQ ID NO:44
21. = Apo B-100 region 11. aa(4177-4267)	SEQ ID NO:45

FIG. 3C

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Comparison of the Apo B-100 SH1-like Region to SH1 Kinase
 Domains of Known Signal Transduction Proteins.

	10	20	30	40	50	60	
V	G	*	**	N*	VA	K *	P T* VPE *E* *K * *V *
APOB	VSDGIAALDL	-----NA-----	VANK	IADFELP	TIIVPEQTI	EIPSIK	FSVPAGIVIPSF
SRC	LGQCGFG	EVWVG	TWNG	T--TRVAIKTLK	-----PGTMS	PEAF	QEAQVMKKLRH-EKLV----
CFYN	LGNGQFG	EVWVG	TWNGNT	---KVAIKTLK	-----PGTMS	PESF	EEAQIMKKLKH-DKLV----
HCK	LGAGQFGE	VWMA	TYN	---KHTKVAVKTMK	-----PGMSV	EAF	LAEANVMKTLQH-DKLVKLH-
LYN	LGAGQFG	EVWVG	YN	NS--TKVAVKTLK	-----PGTMSV	QAF	LEEANLMKTLQH-DKLVRL-Y
LCK	LGAGQFG	EVWVG	YNG	---HTKVAVKSLKQ	-----GSMS	PDA	FAEANLMKQLQH-QRLVRL-Y
	70	80	90	100	110	120	130
	***	****	* P*Y *T *	* K *** *L	** *	** *	I *G
APOB	QAL	TARFEVDS	PVYNAT	WSASLKNKADYVETVL	--DSTCS	STVQFL	---EYELNVLGTHKIEDG
SRC	Q-LY-A	VVSEEP	IYIVTEY	MS-KG-S	LLD-FLK	GET-G-K	---YLRLPQL-VDMAAQ--IASG
CFYN	Q-LY-A	VVSEEP	IYIVTEY	MN-KG-S	LLD-FLK	DGEG-RAL	---KLPNL-VDMAAQ--VAAG
HCK	-AWT-K	---E	PIYIITEF	MA-KG-S	LLD-FLK	SDE-GSKQP	-LPKL-----IDFSAQ--IAEG
LYN	-AWT-R	---E	EPIYIITEY	MA-KG-S	LLD-FLK	SDEGG-KVL-LPKL	-----IDFSAQ--IAEG
LCK	-AWT	-----Q	EPIYIITEY	MEN-G-S	LVD-FLK	TPSGI-K-LTINKL	-----LDMAAQ--IAEG

FIG. 4A

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COMPARISON OF THE Apo B-100 SH1-like Region to SH1 Kinase
 Domains of Known Signal Transduction Proteins.

	140	150	160	170	180	190
	*A	* **HRD*	*A**	* **	K* * GL	*E* *G A** IK *
APOB	TLA-SKTKGTLAHRDF	SAEY---	EEDG----	KF-E-GL-----	QEW---	EGKAHLNIK-S-P-
SRC	-MAYVE-RMNYVHRDLRAANILVGE-N--	LVCKVADFGLARLI	-EDNEYTARQG-AKFPIKWTAPE			
Cfyn	-MAYIE-RMNYIHRDLRSANILVG--	NG-LICKIADFGLARLI	-EDNEYTARQG-AKFPIKWTAPE			
HCK	-MAFIEQR-NYIHRDLRAANILVS---	ASLVCKIADFGLARVI	-EDNEYTAREG-AKFPIKWTAPE			
LYN	-MAYIE-RKNYIHRDLRAANVLVSE---	SLMCKIADFGLARVI	-EDNEYTAREG-AKFPIKWTAPE			
LCK	-MAFIEER-NYIHRDLRAANILVS--	D-TLSCKIADFGLARLI	-EDNEYTAREG-AKFPIKWTAPE			

	200	210	220	230	240	250	260
	A* **	** K D	GI *	** *	P *G **	** ** *	** Y P PD
APOB	AFTDLHLRYQ-K-DKK--	GI--S--	TSAA-SPAVG-TVGM	MDMEDDDFSKWNFY	SPQSS--	PD	
SRC	AAL-Y-GRFTIKSDVWSFGILLTELTTKGRVPYPGM-VNREVLDQVE--	R--GYRMP---	CPPE				
Cfyn	AAL-Y-GRFTIKSDVWSFGILLTELVTKGRVPYPGMN-NREVLEQVE--	R--GYRMP---	C-PQ				
HCK	AI-NF-GSFTIKSDVWSFGILLMEIVTYGRIPYPGMS-NPEVIRALE--	R--GYRMPR----	PE				
LYN	AI-NF-GSFTIKSDVWSFGILLYEIVTYGKIPYPGRT-NADVMTAL--	S--QGYRMPRVENC	PD				
LCK	AI-NF-GSFTIKSDVWSFGILLTEIVTHGRIPYPGMT-NPEVIQNL	E--R--GYRMVR----	PD				

FIG. 4B

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Identification of the Apo B-100 SH1-like Region and
 the SH1 Kinase Domains of Known Signal Transduction
 Proteins and Their Corresponding Sequence
 Identification Numbers

Reference Protein	Sequence ID No.
ApoB (aa 3804-4006)	SEQ ID NO:46
SRC (aa 275-488)	SEQ ID NO:47
FYN (275-488)	SEQ ID NO:48
HCK (268-480)	SEQ ID NO:49
LYN (252-469)	SEQ ID NO:50
LCK (250-462)	SEQ ID NO:51

FIG. 4C

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The Inter-Kringle Proline-Rich Regions of Apo[a] are Compared to
 Proline-Rich Region of SH3-Binding Protein 1 (3BP1).

3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr2	-SDAEG-TAVAPPTVTPVSLEAPSE-QA-----PTEQR-PGVQE	SEQ ID NO:58
3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr3	-SDAEG-TAVAPPTITPISLEAPSE-QA-----PTEQR-PGVQE	SEQ ID NO:59
3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr4	-SDAEW-TAFVPPNVILAPSLEAFFE-QA-----L-TEE-TPGVQD	SEQ ID NO:60
3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr5	---L-V-TE---SSVLATLTVVPDPST-EASSEEA ^U PTEQ-SPGVQD	SEQ ID NO:61
3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr7	P--VMESTLLTTPTTVVPVPSTELPSE-EA-----PTEN-STGVQD	SEQ ID NO:62
3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr8	P--VTESSVLTTPTVAPVPSTEAPSE-QA-----PP-E-KSPVVQD	SEQ ID NO:63
3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr9	-SETE--SGVLET--PTVVP-E-PSM-EAHSEAA ^U PTEQ-TPVVRQ	SEQ ID NO:64
3BP1	TS-LRAPT-MPPP-LPPVPP-Q-PARRQSRR--LPA---SPVIS	SEQ ID NO:57
ikr10	-SDTESGTVVAPPTV--I---QVPSL-----GPPSEQD-	SEQ ID NO:65

FIG. 5A

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Identification of the Inter-Kringle Proline-Rich Regions
 of Apo[a] and the Proline-Rich Region of SH3-Binding
 Protein 1 (3BP1) compared in FIG. 5A.

Reference Protein	Sequence ID No.
3BP1	SEQ ID NO:57
Proline-Rich Region of Sh3-Binding protein 1	
ikr2 amino acids (106-141)	SEQ ID NO:58
ikr3 amino acids (3322-3357)	SEQ ID NO:59
ikr4 amino acids (3436-3471)	SEQ ID NO:60
ikr5 amino acids (3550-3585)	SEQ ID NO:61
ikr7 amino acids (3770-3805)	SEQ ID NO:62
ikr8 amino acids (3884-3919)	SEQ ID NO:63
ikr9 amino acids (3998-4033)	SEQ ID NO:64
ikr10 amino acids (4112-4137)	SEQ ID NO:65

FIG. 5B

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Proteins Are Compared to the Analogous Regions in Apo B-100.

	*K*A***	R*	****	**	**G*	G***	*	*	***	
B100(13-49)	PKDATRFKHLRKTYNYEAESSGV-PGTAD--	SRSATRI	(SEQ	ID	N0:66)					
SRC(7-40)	PKDAS----	QRRRSLEP-AENVHGA-GGGAFPASQTPSKP	(SEQ	ID	N0:67)					
FYN(7-38)	DKEATKLTEERDGS LN---	Q-SSG RYRG T-DP---	TPQHY	(SEQ	ID	N0:68)				

FIG. 6A

	***	*	TF	Y*	*L	*	**T	*P	Y	PGE	L
apoB-100 (4448-4536)	IQNYH-TFLIYITELLKKLQSTTVMNP-YMKLAPGE-LTIIL	(SEQ	ID	N0:69)							
SRC(505-535)	PEE-RPTF-EYLQAFLEDYFTST--	EPQYQ---	PGENL----	(SEQ	ID	N0:70)					
FYN(506-536)	PEE-RPTF-EYLSFLEDYFTAT--	EPQYQ---	PGENL----	(SEQ	ID	N0:71)					
HCK(498-526)	PEE-RPTF-EYIQSVLDDFYTAT--	ESQYQQQ-P-	-----	(SEQ	ID	N0:72)					
LYN(483-511)	AEE-RPTF-DYLSVLDIFYTAT--	EGQYQQQ-P-	-----	(SEQ	ID	N0:73)					
LCK(480-508)	PED-RPTF-DYLSVLEDDFYTAT--	EGQYQPQ-P-	-----	(SEQ	ID	N0:74)					

*indicates conserved amino acids

FIG. 6B

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Examples of Proline Pipe Helix Structures in ApoB-100

SEQ ID NO:	Sequence	Sequence Source
77	PQNAKLKIKRPVKVQPIARVWY	Tus proline pipe (223-243)
78	PDFRLPEIAIPEFIIPTLNLND	ApoB-100 (2682-2702)
79	NDFQVPDLHIPEFQLPHISHTI	ApoB-100 (2702-2723)
80	PSLELPVLHVPRNLKLSLPHFK	ApoB-100 (3273-3294)

FIG. 7

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Sequence Comparison of DNA-Binding Protein ISGF3 γ SEQ ID
 NO:81, and a Similar Region of Apo B-100 SEQ ID NO:82,
 Located Between Residues 0008 and 0393.

MAS--GRARCT--RKLRNWVEQVESGQ---FPGVCWDDTA-KTMFRI	ISGF3 γ
VSLVCPKDA-TRFKHLRKTYN-YEAESSGVPGTADSRATRINCKV	apoB100
** * T **LR * ** *E* *PG *A * **	
PW--KHAGKQDFRESQDAAFFKAWAIF----KGKYK---EGDKVPER	ISGF3 γ
ELEVPLCSFILKTSQCTL--KEVYGFNPEGKALLKTKNSEEFAAAM	apoB100
* * ** SQ ** K ** F K* *K* * * **	
GRMDVAEPYKVYQLPPG-IVSGQPGTQKV-PS-----KQHSVSSE	ISGF3 γ
SRYE----LKL--AIPEGKQVFLYP--EKDEPTYILNIKRGIIISALLV	apoB100
R** *KV **p G V P *K* P* KR S*	
RKE-EDAMQNCTLSPSVLQDSLNNEEGASGGAVHSDIGSSSSSSPEP	ISGF3 γ
PPETEEAKQVL-FLDTVYGNCSHTFTVKTRKGNVATEISTERDLGQCD	apoB100
E E*A Q * *V* * * * * S*	
QEVTDTEAPFGQDQRSLEFLPPPEPDYSLLLTFIYNGRVVGEAQVQS	ISGF3 γ
RFKPIRTGISPLALIKGMTRPLSTLISSSQSQYTLDAKRKHVAEAI	apoB100
T * * * * * * *L * S * **** A**	

FIG. 8A

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Sequence Comparison of DNA-Binding Protein ISGF3 γ SEQ ID
 NO:81, and a Similar Region of Apo B-100 SEQ ID NO:82,
 Located Between Residues 0008 and 0393.

LDCRLVAEPSGSESS-ME-QVLF-PKPGPEPTQRLLSQLERGILVASN KEQHLFLPFSYKNKYGMVAQVTQTLKL--EDTPKINSRFFGEGTKKMG -* L ** *S - * M QV *K* E T ** S - *	ISGF3 γ apoB100
PRGLFVQ--RLCPIPIISWNAPOAPPGPGLLPSNECVELFRTAYFCR ---LAFESTKSTSPPKQAEAVLKTQLQELKLTISEQNIQ--RANLFNK L *** * * *p- *A* - * - *L *S** ** R* *F *	ISGF3 γ apoB100
DLVRYFQGLGPPPKFQVTLNFWEEHSGSHTPQNLITVKMEQAFARYL -LVTELRLGLSDEAVTSLLPQLIEVSSPIT-LQALVCGGPQCSTHIL LV *GL * * * ***E S * *Q L* Q ** *L	ISGF3 γ apoB100
KMEQAFARYLLEQ-TPEQQAAILSLV KRVHANP-LLIDVVTY---LVALIPE K -A * L** T* ***L *	ISGF3 γ apoB100

* indicates conserved amino acids
 bold type indicates positively charged, basic amino acids

FIG. 8A Cont.

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Sequence Comparison of DNA-Binding Protein ISGF3 γ SEQ ID
 NO:81, and a Similar Region of Apo B-100 Located Between
 Residues 2930 and 3324, SEQ ID NO:83.

MA-SGRARCTRKLNRNVVEQVESGQFPGVCWDD-----	ISGF3 γ
FGLSNKIN-SKHLRVNQNLVYESGSLNFSKLEIQSQVDSQHVGHSVL	apoB100
** S ** **LR **ESG * **	
TAKTM-----FRIPW--KHAGKQDFRESQDAAFFKAWAIFKGYKEG	ISGF3 γ
TAKGMALFGEKAEFTGRHDAHLNGKVIG-TL--KNSLFFSAQPFEI	apoB100
TAK M ** * **H ** * ** K **F	
---DKEVPE-RGRMDVAEPYKVYQLPPGIVSGQPGTKVPSKRQHS	ISGF3 γ
TASTNNEGNLKVRFPRLTGKI-DFLNNYALFLSPSAQQA-SWQVSA	apoB100
* * * R* * * K* **L ** * P *Q * S	
KRQHSSVSSE---RKEEDAMQNCTLSPSVLQDSLNNEEGASGGAVHS	ISGF3 γ
RFNQKYKNQNFSA GN ENIMEAHVGINGEANLDFLNI-PLTIPEMR-	apoB100
* * - * * *E**M* ! ** * N ** **	
DIGSSSSSSPEPQEVTDTEAPFQQDQRSLEFLPPEPDYSLLLTF	ISGF3 γ
-LPYTIITTPPLKDFSLWEKTGLKEFL-KTTKQSFDSLVAQYKKNK	apoB100
* * * ** p - * \ / ** * * * * *	

FIG. 8B

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Sequence Comparison of DNA-Binding Protein ISGF3 γ SEQ ID
 NO:81, and a Similar Region of Apo B-100 Located Between
 Residues 2930 and 3324, SED ID NO:83.

IYNGRVGEAQVQSLDCRLVAEPGSESSMEQVLFPKPGPEPTQRL
 HRHSTNPLAVLCEFISQSIKSFDRHFEKRNNDLDFVTKSYNETKIK
 * * * * * E - * * * * *

ISGF3 γ
 apoB100

SQLERGILVASN-PRGLFVQRLCPIPIISWNAPOAPPQPGPHLLPSNE
 FDKYKAESHDELPRT-FQIPGYTPV-VNVEVSPFTIEMSAFGYVF
 * - * - * * PR F\ / * p * * N * p * * *

ISGF3 γ
 apoB100

CVELFRTAYF--CRDLVRYFQGLGPPPKFQVTLNFWEEHSGSSHTP
 -PKAVSMPSFSILGSD-VRVPSYTLILPSLELPVLHVPRNKLSTPH
 * - * * * * F D VR * * * * * - * - * S

ISGF3 γ
 apoB100

-QNLITVKMEQAFARYLLEQTPEQQAAILSLV
 FKELCTISHIFIPAMGNITYDFSFKSSVITLN
 - & L T * - * * A * * - * * * * * L

ISGF3 γ
 apoB100

* indicates conserved amino acids
 bold type indicates positively charged, basic amino acids
 ISGF3 γ = sequence ID No:81. Apo B-100 amino acids (aa
 2930-3324) = sequence ID NO:83.

FIG. 8B Cont.

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Various regions of apoB-100 having similarity of ISGF3 γ (1-51)

SEQ ID NO:		
84	ISGF3 γ (1-51)	MASGRARCTRLRNWVVEQVESGQFPGVCWDDTAKT $\overline{\text{MFRIPWKHAGKQDFR}}$
85	APOB(13-59)	--PKD $\overline{\text{ATRFKHLRKYTYNYEAESSGVPGTAD-SRSATRINCKVELEVLPQ}}$
86	APOB(80-116)	--PEGKALLK $\overline{\text{TKNSEFAAAM}}\text{-----SRVELKLAIP-EGKQVFL}$
87	APOB(159-196)	--CSTHFTV $\overline{\text{KTRKGNVATEIST}}\text{-----ERDLGQCDRFKPIRTGIS}$
88	APOB(363-413)	CSTHILQWL $\overline{\text{KRVHANPLLIDWVTVLVAIPEPSAQLREIFNMARDQRSRA}}$
89	APOB(1082-1119)	HLSCDTKEERK $\overline{\text{IKGVISI}}\text{-----PRLQAEARSEILAHWSPAKL}$
90	APOB(1441-1487)	--SVHLDSKKKQHL $\overline{\text{FVKEVKIDGQFRVSSFY--AKGTYGLSCQDPNTGRL}}$
91	APOB(2073-2113)	KHINIDQFVRKYRAALGKL $\overline{\text{PQQANDYLSFNWERQVSHAKE}}\text{-----}$
92	APOB(2114-2153)	---KL $\overline{\text{TALTKKYRITENDIQIA}}\text{-----LDDAKINFNEKLSQLQTYMIQ}$
93	APOB(2281-2330)	-ERINDVLEHV $\overline{\text{KHFVINLIGDFEVAEKINAFRAKVHVELIERYEVDQDIQVL}}$
94	APOB(2390-2439)	-NKFLDMLIK $\overline{\text{KLKSFYHQFVDETNDKIREVTQRLNGEIQALELPQKAEAL}}$
95	APOB(2933-2955)	----SNK $\overline{\text{INSKHLRVNQNLVYESGSLN}}\text{-----}$
96	APOB(2956-3001)	-----FSKLEIQSQVDSQH $\overline{\text{VGHSVLTAKGMALFGEKGKAEFTGRHDAHLNGK}}$

FIG. 9A

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VARIOUS REGIONS OF APOB-100 HAVING SIMILARITY OF ISGF3 γ (1-51)		SEQ. ID NO.
-VKAQYKKNKRRHSITNPLAVLCEFISQSIKSFD RH FEKRN N NALDFVTKS	APOB (3146-3195)	97
KLEGTTRLTRKRG L KLATALSLSNKFVEGSHNSTVSLTTKNMEVSVAKTTK	APOB (3353-3403)	98
KLDVTTSIGRRBQH L RVSTAFVYTKNPNGYSFSIPVKVLADK F ITPGLK L ND	APOB (3662-3712)	99
--FBEIQYK K LRYSSFALN L PTLPEVKFPEVDVLT K YSQPEDSLIPF E I	APOB (3738-3786)	100
---LHLRYQ K DKKGGISTSAASPAGTVGM D MD E DD D DFSKWNFY S SPQSSPD	APOB (3959-4006)	101
---LREVSSK L RRNLQNNAEWVYQGAI R QID I DVRFQKAASGTTGT Y QEW	APOB (4070-4117)	102
-RVTQKFHMKVKHLIDSLIDFLNFRFQFPGKPGIY T REELCTMFIREVGT	APOB (4150-4119)	103

FIG. 9A Cont.

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Various regions of apoB-100 having similarity of ISGF3 γ (42-69)

	SEQ ID NO:
WKHAGKQDFRESQDAFF-----KAWAIFKGYK $\overline{\text{EG}}$ -DKEVPERGRMDVAEPYK	104
EHVKHFVINLIGD-----FEVAEKINA-FRAKVHELIEREYVDQQIQVLM $\overline{\text{DKLV}}$	105
VRKYRAALGKL PQQANDYLSFNWERQVS--HAK $\overline{\text{EKL}}$ TALTKKYRITENDIQIA	106
YIKSYDLHDLKIAIANIIDEIIEKL $\overline{\text{KSL}}$ DEHYH $\overline{\text{IRVNL}}$ VKT $\overline{\text{IHDLHL}}$ FIEIDFNK	107
-----KITL $\overline{\text{IINWL}}$ QEALSSASLAHMKAK $\overline{\text{FRETL}}$ EDTR-----	108
-----TDHFSLRARYHMKADSVVDLSYNVQSGSETTY	109
-----KLTTNGRFREHNAK $\overline{\text{FSLDGK}}$ -----	110
DTKYQIRIQIEKLQQLKRHIQNI $\overline{\text{DQHL}}$ AGKLKQHIEAIDVRVLLDQLGTT-----	111
-----FHDFPDLGQEV $\overline{\text{ALNANTKNQIRW}}$ KNEVR $\overline{\text{IHSGSFQSQV}}$ ELSNDQ-	112
-----KDNVFDGLVRVTQ $\overline{\text{KFHMKV}}$ KHLIDSLIDFLNFP $\overline{\text{R}}$ -----	113
-----HRNIQEYLSILTPDGK $\overline{\text{GKEK}}$ IAELSATAQEIIKS-----	114

FIG. 9B

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Sequence Comparison of DNA-Binding Domains of SREBP 1 (aa 279-452) SEQ ID NO:116, SREBP 2 (aa 287-568) SEQ ID NO:117 and ADD1 (aa 250-421) SEQ ID NO:118 to a Similar Region of Apo B-100 (aa 2024-2234) SEQ ID NO:115.

EFTIVAFVKYDKNQDVHSINLPFFETLQEFERNRQTIIWLVNQ	APOB100
GPLPTLVSGGTILATVPLVDAEKLPIINLAAGSKAPASQSR-GE	SREBP1
QVPTLVGSSGTTITMPVMGQEKVPIKQVPGGVKQ-LEPPKE-GE	SREBP2
GPLQTLVSGGTILATVPLVVDTDKLPIDHRLAAGGKALGSAQSR-GE	ADD1
***** V * * * ***** *Q * ** E *	
RKCLKHINIDQFVRKYRAAL-GKLPQQANDYLSFNWERQVSHAKEK	APOB100
KRTAH-NAIE--KRYRSSINDKIIELK-DLVGTEAKLNKSAVLRK	SREBP1
RRTH-NIE--KRYRSSINDKIIELK-DLVGTDAKMHKSGVLRK	SREBP2
KRTAH-NAIE--KRYRSSINDKIVELK-DLVGTEAKLNKSAVLRK	ADD1
R* H NI * **YR*** K*** D** * * S * K	
LTALTKKYRITEND-IQIALDDAKINFNEKLS-----QLQTYMIQF	APOB100
AIDYIR-FLOHSNOKLQDENLSRTAV-HKSKSLK--DLVSAC---	SREBP1
AIDYIK-YLQQVNHKLRQENMVLKLA-NQKNKLLKGIDGLSLV---	SREBP2
AIDYIR-FLOHSNOKLQDENLTLRSA--HKSKSLK--DLVSAC---	ADD1
* * K Y N* * *K* *N*K *L ***	

FIG. 10A

DQYIKDSYDLHD-LKIAIANIIDETIEKLKSLDEHYHIRVILVKTI APOB100
GSGG-NTDVLMEGVK-----SREBP1
DN-----EV-D-LKI-----SREBP2
GSGGG-TDVSMEGMKP-----ADD1
D* ** ** D LKI

```

HDLHLFIENIDFN-----KSGSSTASWIQNVDTKYQIRIQ  APOB100
-----TEVEDTL--TPPP-SDAGSPFQSSPLSLGSRGSGSGG  SREBP1
-----E-DFNQNVLLMSPPASDSGSQAGFSPYSIDSEPGSPLL  SREBP2
-----EVVETL--TPPP-SDAGSPSQSSPLSLGSRGSSSGG  ADD1
      *  DFN          SGS *** *  *D* *  *

```

FIG. 10A Continued

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Sequence Comparison of SREBP1 to Apolipoprotein apo A1
 apoA1 (1-243) SEQ ID NO: 119 and SREBP1 (aa 233-500) SEQ ID NO:120

DEPPQSPWDRVKDLATVYVDVLKDSGRDYVSQFEGSALGKQLNLKLLDNWDSVTSTFSKLREQLGPVTQEFWDN	apoA1
QQVPVLLQPHFTIKADSLLLTAMRTDGATVK-----AAGLSPLVSGTTVTG-PLPTLVSGG--TILATVPLVVD-	SREBP
p * **~* * **K~/G **~ ***L * ** * * *S * *~/ **D	
LEKETGLRQEMSKDLEEVKAKVQPYLDQFQKKWQEMELYRQKVEPLRAELQEGARQKLHELQ-EKLSPLGEE	apoA1
AEKLPINRLAAGSKAPASQSRG-----EKRTAHNAIEKRYRSSINDKIIELKDLVVGTEAKLNKSAVL---	SREBP
*EK V/ SK * * **~ *K~/R ~ **~ *K ***	
MRDRAR--AHVDALRTHLAPYSDELQRQRLAARLEA-LKEN-----GGARLAEY-HAKATE-----	apoA1
-R-KAIDYIRF-LOHSNQKLKOENLSLRTAVHKSLSKLDLVSAAGSGGNTDVLMEGVK-TEVEDTLTPPPSDAG	SREBP
R~*A *** * **~ *~*~L R ***~L~*	
-----HLSTLSEKAKPALEDLRQGLLPVLESFKVSFLSALEYTKK--	apoA1
SPFQSSPLSLGSRGSGGSGDSEPDSPVF-----EDSKAKP--EQ-RPSLHSGMLDR-SRL-ALCTLVFLC-	SREBP
~/KAKP E* R L ~S L AL *	
LNTQ	apoA1
LSCN	SREBP
L *	

FIG. 10B

apoA-II
SREBP1

FIG. 10C

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Sequence Comparison of apoAIV (30-376) SEQ ID NO:123 and SREBP1 (aa 330-1146) SEQ NO:124

QKSEL	TQQLNAL	FQDKL	GEVNTYAGD	LQKLV	PFATEL	HERLAKD	SEKLKEE	IQKELE---	ELRA-R-LLPH	apoAIV	
EKLPI	-NRLAAGS-	-KAPAS	AQSRGE-	-KRTAH	NAIEKRY	SSIN-DKI	TE-L-KDL	VVGTEAKLN	KSAYLR	SREBP1	
*R	* * L A	R*	G* R* *	A E *	R * *	*R* E *	R*L	E*** *	***		
-ANEV	SQIGDNL	RELQ	RPYADQL	RTQVNT	QAEQL	RRQLD	PLAQ--	-RMER	VLRNADS-LQASLRPH--	apoAIV	
KAIDY	-IRFLQHS-	-NQKL	KQENLS	RTAVH	KS-K	-DLVS	ACGGNTD	VLMEGV	KTEVEDTLTPPPR	SREBP1	
A **	** *	*Q*	LRT V	L* *	*L *	VL E	* ** *	*L P			
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----		
DAGSP	FQSSPL	SLGR	SGSGSD	SEDP	SFEDS	KARPE	QRP-SLH	SR---GML	DRSLALCTLVFLC	apoAIV	
						** KAR**	Q* L*	R *	* ** T*	SREBP1	
RSLAP	YAQDTQ	EKLNHQ	LEGLTFQ	MKKNAEEL	KARISASAE	ID-QTVEEL	RRSLAPYAQD	TQEKLNHQ	LEGL	apoAIV	
LSCN	PLASLL	GARGL	PSPSDTT	SVYHSP	GRNV	EGTESR	DGPGWAQV	QLFCDLL	LVRTSLWRQQ-QPPAP	SREBP1	
S P*A	*	T	** *	* ** *	S *	QV*	* L***	* *	* * Q* **		
TFQMK	NAEEL	KARISASAE	ELR--QR---	LAP	AEDVR	GNLKGNT--	EGLQKSLAE	LGGHLDQQVEE--	-F	apoAIV	
APAAQ	GASSRP---	QASALE	IRGFQ	RDLS	SLRRLA	QSF	RPAMRRV	FLHEAT	ARLMAGASPTRTHQLLDRSL	SREBP1	
**	* *	ASA ELR	QR	L	LA* *	R *	**	E*	* * A *		
RRRVE	PGENFN	KALVQ	QMEQL	RQKL	GPHAGD	VEGHL	S-FLEK	----LRD	KVNSFFSTFKEKESQ-DKTL	apoAIV	
RRRAG	PGGKG	--AVAE	-LE-PR	PT	RRHA-EALL	ASCYL	PPGFL	SAPGQ	RVGM	LAEAARTTEKLGDRRL-	SREBP1
RRR*	P G	A*** *	E *R	HA **	*S *	L	* **V	* *	* * E *	D* L	

FIG. 10D

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Sequence Comparison of apoAIV (30-376) SEQ ID NO:123 and SREBP1 (aa 330-1146
 SEQ ID NO:124

apoA.
 SREBI

LPELEQQEQQEQQEQVQMLAPLES
 LHDCQQ-----MLMRLGGGTTVTSS
 L-* *Q ** S

FIG. 10D Cont.

Sequence Comparison of acat (fragment 1) SEQ ID NO:125 and SREBP1
 (aa 300-486) SEQ ID NO:126

EKMSLRNRLS-KSRENPEEDED-QRNPAKESLETPSNGRIDIKQLIA
 EKLPINRLAAGSKAPASAQSRGEKRTAHNAIE-----
 ER* * NRL* S* * * A***E
 acat
 SREBP1

KKIKLTANGRI-DIKQLIAKK-IKLTAEINGRIDIKQLIAKKIKLTAE
 KRYRSSINDKIIELKDLVVGTEAKLNKSYIRFLOHS--NQKLQENL
 R*** **N *I **K*L** *KL R*//* K*K
 acat
 SREBP1

AEELKPFFMKEVGVSHFDDFVT-----NLI-EKSAS-LDNKAHSF
 S--LRTAVHKSKSLK--DLVSACGSGGNTDVLMEGVKTEVEDKAKPE
 * L***K * D*V* *** E * ***KA*
 acat
 SREBP1

VRENV-PR-VLNSAKEK
 QRP SLHSRGMLD--RSR
 R * R *L* * *
 acat
 SREBP1

FIG. 10E

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Sequence Comparison of acat (fragment 2) SEQ ID NO:127 with
 SREBP1 (aa 1061-1085) SEQ ID NO:128

RRHC-PLKNPTFLDYVRPRSWTCRYVF	acat
RRRAGPGGKGGAVAELEPRPTRREH	SREBP1
RR* p ** * PR	

FIG. 10F

Sequence Comparison of apoE (aa 124-181) SEQ ID NO:129 and SREBP1 (aa 302-360) SEQ ID NO:130

AMLGQSTEE-LRVRLA--SHL-RKLRKRLRDADDLOKRL-AVYQAGAREGAERGLSAIRE-RL	apoE
KLPINRLAAGSKAPASAQSRGEKRT----AHNA--IEKRYRSSIN--DKIIELKDLVVGTEAKL	SREBP1
** * ** ** S* ** **** **KR* * ** * \/* L * E *L	
--GPLVEQGRVRAATVGSLAGOPLQERAQAWGERLRARMEEMGSRT-RDRLDEVKEQVA	apoE
NKSAVL---R-KAIDYIRFLQHSNQKCKQENLS-LRTAVHK--SKSLKD-LVSACGSGG	SREBP1
*** R KA* * ** Q LR* S** D 1 * *	

FIG. 10G

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Sequence Comparison of apoC-II (aa 1-42) SEQ ID NO:131 with
 SREBP1 (aa 231-275) SEQ ID NO:132

TQQPQQDEMPSTFLTQVK-----ES--LSSYE---SAKTAQNLYEKTYL	apoC-II
SQ-IQQ-----VPVLLQPHFIKADSLLLTAMKTDGATVKAAGLSPLVSGTT	SREBP1
*Q *QQ * *L Q** *S L*** **K*A* **	

FIG. 10H

Sequence Comparison of apoC-III (aa 7-51) SEQ ID NO:133 with
 SREBP1 (aa 314-360) SEQ ID NO:134

SLLSFMQGYMKHATKAKDAL--SSVQESQVAQQARGWVTGDFSSLK--	apoC-I
APASQSRGEKRTAHNAIEKRYRSSIND-KIIE-LKDLVVGTEAKLNKS	SREBP1
S K A * SS*** *** ** *L	

FIG. 10I

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Sequence Comparison of APO C-III (aa 52-79) SEQ ID NO:135 with
 SREBP1 (aa 717-748) SEQ ID NO:136

DYWT--VKDKFSEFWDLDPEVRP--TSAAVAA	apoC-III
EIYVAAALRVKTSLPRALHFLTRFFLSARQA	SREBP1
*** * ** R S * L * R * *SA A	

FIG. 10J

Sequence Comparison of apo D (aa 30-34) SEQ ID NO:137 with SREBP1
 (aa 301-305) SEQ ID NO:138

EKIPT	apoD
EKLPI	SREBP1
ER*P	

FIG. 10K

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Sequence Comparison of apo D (aa 36-65) SEQ ID NO:139 with SREBP1
(aa 361-391) SEQ ID NO:140

ENGRCIQANYS-LME-NGKIKVLNQELRADG	apoD
AVLRKA-IDYIRFLQHSNQKIKQENLSRTAV	SREBP1

FIG. 10L

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Comparison of the Primary Structures of Known Coiled-Coil Regions of
 DNA-Binding Proteins and Analogous Regions in Apo B-100

MKQLEDKVEELL	SKNYHLENEVARLKKLVGER	GCN4-p1	(SEQ ID NO:141)
KHEIQEMFDQL	RAKEKELRTWEEELTRAALQQ	hMLK1(286-317)	(SEQ ID NO:142)
EELLRRREQEL	AEREIDILERELNIIHQLCQ	hMLK1(321-352)	(SEQ ID NO:143)
RIQIEKLQQL	KRHIQNIHQHLAGLKHIE	apoB(2232-2264)	(SEQ ID NO:144)
VLQQVIKDYFEKL	VGFIDDAVKKLNELSFKTFIE	apoB(2353-2387)	(SEQ ID NO:145)
ELSFKTFIEDV	NKFLDMLIKKLKSFQYHQFV	apoB(2379-2409)	(SEQ ID NO:146)
HQFVDETNDK	IREVTRQRLNGEIQALELP	apoB(2406-2433)	(SEQ ID NO:147)
AAKNLTDFAEQYS	IQDWAKRMKALVEQGFTV	apoB(2530-2560)	(SEQ ID NO:148)
SASLAHMKAKF	RETLEDTRDRMYDMDIQQLQRYL	apoB(2475-2509)	(SEQ ID NO:149)
CLNLHKFNEFI	QNELQEASQELQIQHYIMALREE	apoB(4326-4360)	(SEQ ID NO:150)
FLIYITELLKK	LQSTTVMPYMKLAPGELTIIL	apoB(4504-4536)	(SEQ ID NO:151)

FIG. 11

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Comparison of Known ATP-Binding Loop Motifs to Similar Regions in Apo B-100. The critical amino acid H is indicated by (#)

A: THE HIGH LOOP		
RLLDHRVPETDMTFRHVGSKLIVAMSSWLQ	apoB(1183-1212)	(SEQ ID NO:152)
LNFSKLEIQSQVDSQHVGHVSLTAKGMALF	apoB(2954-2983)	(SEQ ID NO:153)
NQNFSAAGNNENIMEAHVINGEANDLFLNI	apoB(3072-3101)	(SEQ ID NO:154)
MVVTRIAPSPT-GDPHVGTAIYIALFNYAWA	TTETS(1-29)	(SEQ ID NO:155)
TTVHTRFPPEPNGYLHIGHAKSICLNFGIA	ECQTS(25-54)	(SEQ ID NO:156)
KIKLYCGVDPTAQSLHLGNLVPMLLHFYV	YSCMSY1(85-114)	(SEQ ID NO:157)
PIALYCGFDPTADSLHLGHLVPLLCLKRGQ	ECOTYRS(33-62)	(SEQ ID NO:158)
RVTLYCGFDPTADSLHIGNLAAIILTLRRFQ	BACTYRSA(30-59)	(SEQ ID NO:159)
RIGAYVGIDPTAPSLHVGHLPLMPLFWMY	NEUTYRSM(95-124)	(SEQ ID NO:160)
PIALYCGFDPTADSLHLGHLVPLLCLKRFQ	SYE ECOLI(31-61)	(SEQ ID NO:161)
PLKVKLGLGADPTAPDIHLGHTVVLNKLRLQFQ	HEAHI1610(31-60)	(SEQ ID NO:162)

#

FIG. 12A

Comparison of Known ATP-Binding loop Motifs to Similar Regions in Apo B-100. The critical amino acid K is indicated by (#)

B: THE KMSK LOOP

VSKGLLIFDASSMGPMASVHLD SKKKQLFVKEVKIDGQF	apoB(1421-1463)	SEQ ID NO. 163
TIITTPPLKDFSLWEKTLKEFLKTTKQSFDSLVAQYKKNKH	apoB(3113-3155)	SEQ ID NO. 164
KNRNALDFVTKSYNETK----IKFDKYKAEKSQDELPRTFQI	apoB(3183-3221)	SEQ ID NO. 165
DALQYKLEGTRL---TR----KRGLKLATALSLSNKFVEGSH	apoB(3348-3390)	SEQ ID NO. 166
RAFGWEAPREYHMPLLRNPDK-TKISKRKSHSTSLDWYKAEGL	ttets(221-262)	SEQ ID NO. 167
DNITIPVHPRQYEFRLNLEY-TVMSKRKLNLLVTDKHEGVWD	ecqts(245-287)	SEQ ID NO. 168
KNKGL--PFGITVPLLTATGE-KFGKSAGNAVFIDPSINTAY	YSCMSY1(282-320)	SEQ ID NO. 169
RLHQNQ-VFGLTVPLITKADG-TKFGKTEGGAVWLDPKKTSFY	ECOTYRS(215-254)	SEQ ID NO. 170
KTKGEARAFGLTIPLVTKADG-TKFGKTESGTIWLDEKETSFY	BACTYRSA(210-249)	SEQ ID NO. 171
KTALDE-CVGFTVPLLTDSG-AKFGKSAGNAIWLDPYQTSVF	NEUTYRSM(303-343)	SEQ ID NO. 172
RLHQNQ-VFGLTVPLITKADG-TKFGKTEGGAVWLDPKKTSFY	SYE ECOLI(213-253)	SEQ ID NO. 173
SAGKK-PQVAITLPLLVGLDGEKKMSKSLGNYIGVTEAPSDMF	HEAHI1610(202-243)	SEQ ID NO. 174

#

FIG. 12B

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A COMPARISON OF THE ATP-BINDING SITE WITH GLYCINE LOOP WHICH IS PRESENT IN SRC AND OTHER
 SINGAL TRANSDUCTION PROTEIN SH1 KINASE DOMAINS WITH THE ANALOGOUS SEQUENCE IN THE APO B-100
 SH1 REGION.

RVSTA-F--VY--TKNPNGYSPVVKVLADKFITPGLKL APOB (3676-3710) SEQ. ID NO. 176

KLGGGCFGEVWMGTW--NGT-----TRVAI-KTLKPG SRC SEQ ID. NO. 176

K***G***	NG	VA	K *	#
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FIG. 12B Cont.

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Examples of Nuclear Localization Signal Sequences in the ApoB-100
 Amino Acid Sequence Compared to Known NLS Sequences.

Human apoB-100 sequences with 10 amino acids in the spacer region
 between the bipartite NLS element

SEQ ID NO.	Sequence	Source of Sequence
178	HKNTSTLSCDGLRHKF	human apoB-100 (1387-1403)
179	RKLKHINIDQFVRKYRA	human apoB-100 (2070-2086)
180	RHIQNIDIQLAGLKKQH	human apoB-100 (2244-2261)
181	KKGFYKKKQCRPSKGRK	human IGFBP-3
182	KKPLDGEYFTLQIRGRER	human p53 fragment 1
183	KRALPNNTSSSPQPKKK	human p53 fragment 2
184	KKTNLFSALIKKKKTA	human Ab1
185	RKTLNLSLEEAKKKKED	human apof fragment 1
186	RREDESLOVAERLTRK	human apof fragment 2

FIG. 13A

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Human apoB-100 sequences with 10 amino acids in the spacer region
 between the bipartite NLS element

SEQ ID NO.	Sequence	Source of Sequence
187	RRSYALVSLFFRKLRL	human ir fragment 1
188	RRYGDEELHLCVSRKHF	human ir fragment 2
189	KRVAKRKLIEQNRERRR	human thyroid receptor fragment 1
190	HRSTNAQGSWQRRKF	human thyroid receptor fragment 2
191	KRPPISDSEELSAKKRK	human af9
192	KKGKKPKTEKEDKVKHI	human irf2
193	RKRMNRRIAASKCRKRK	human ap1
IGFBP-3 = interferon growth factor binding protein 3; apoJ = apolipoprotein J; ir-insulin receptor; af9-activation factor 9; irf-insulin response factor 2; ap1 = activation protein 1		

FIG. 13A Cont.

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Human apoB-100 sequences with more or less than 10 amino acids
 in the spacer region between the bipartite NLS element

SEQ ID NO.	Sequence	Source of Sequence
194	RHIQNIDIQHLAGKLKQH	human apoB-100 (2244-2261)
195	KKITEVALMGHLSCDTKEERK	human apoB-100 (1072-1094)
196	KHINIDQFVRKYRA	human apoB-100 (2073-2086)
197	HRNIQEYLSILTDPDGKGKEK	human apoB-100 (4418-4438)

FIG. 13B

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Human apoB-100 sequences with more or less than 10 amino acids in the spacer region between an imperfect bipartite NLS element

SEQ ID NO.	Sequence	Source of Sequence
198	KEVYGFNPEGKALLKGTK	human APOB100 73-90
199	KVLVDHFGYTKDDKHEDM	human APOB100 705-723
200	KAGKLKFIIPSPKRPVKL	human APOB100 891-908
201	RQVSHAKEKLTALTKKYR	human APOB100 2106-2123
202	KYQIRIQIEKLQLKRRH	human APOB100 2228-2245
203	KGMALFGEKGAEFTGRHDAH	human APOB100 2978-2997
204	KQSFDLSVKAQYKKNKHR	human APOB100 3139-3156
205	KLEGTTRLTRKRGLK	human APOB100 3353-3367
206	KLDVTTSIGRRQHLR	human APOB100 3662-3676
207	KLDFREIQIYKKLR	human APOB100 3735-3748

FIG. 13C

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Human apoB-100 sequences with more or less than 10 amino acids in the spacer region between an imperfect bipartite NLS element

SEQ ID NO.	Sequence	Source of Sequence
208	KSPATDLHLRYQDKK	human APOB100 3952-3968
209	KYHWEHTGLTLREVSSKLRR	human APOB100 4060-4079
210	KDNVFDGLVRVTQKFHMKVKH	human APOB100 4141-4161

FIG. 13C Cont.

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ALIGNMENT OF HUMAN 2041-2220 SEQ ID NO:211 WITH PIG SEQ ID NO:212 AND RAT
SEQ ID NO:213 APOB-100 SEQUENCES

SINLPFFETLQEFERNBQTIIVVLENVORKLKHINIDOFVRKYBAALGKLPQQANDYLN	Human (2041-2100)
PPQQVNDYLN	Pig (fragment 1)
KYRVALSRLPQQTHDYLN	Rat (fragment 1)
SFNWERQVSHAKEKLTALTKKYRITENDIQIALDDAKINFNEKLSQLQTYMIQFDQYIKD	Human (2101-2160)
TFSWERQVLSAKKKHSDFMEDYRITENDVRIALDNAKINLNEKLTQLQTYVIQFDQYIKD	Pig (fragment 1)
ASDWERQVAGAKEKLTSMENYRITDNDVLIALDSAKINLNEKLSQLETYAIQFDQYIRD	Rat (fragment 1)
SYDLHDLKIAIANIIDEIIIEKLSLDEHYHIRVILVKTIHDLHLFIENIDFNKSGSSTAS	Human (2161-2220)
NYDLHDFKTAIARIIDEIIATLKIL	Pig (fragment 1)
NYDAQDL	Rat (fragment 1)

FIG. 14A

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ALIGNMENT OF HUMAN 2701-3540 SEQ ID NO:214 WITH HAMSTER SEQ ID NO:215 AND MOUSE SEQ. ID
 NO:216 APOB-100 SEQUENCES

LNDFOVPDLHIPEFQLPHISHTIEVPTFGKLYSILKIQSPLFTLDANADIGNGTTSANEAE	Human (2701-2760)
EFQLPRLSHTIEIPAFGR ^L LHGILKIQSPLFILDANANIQNVTTL ^N ENKAE	Hamster (frag 1)
EFQLPHLSHTIEIPAFGKLHSILKIQSPLFILDANANIQNVTTS ^G GNKAE	Mouse (frag 1)
GIAASITAKGESKLEVLNDFQANAQLSNPKINPLALKESVKFSSKYLRT ^E HGSEMLFFG	Human (2761-2820)
IVASIAAT-GESEIEALNDFQAAQAFLELNP ^N PLILKESMNFSSKHARMEHEGEILFSG	Hamster (frag 1)
IVAS-VTAKGESQFEALNDFQAAQAFLELNP ^H PPVLKESMNFSSKHVRMEHEGEIVFDG	Mouse (frag 1)
NAIEGKSNTVASLHTEKNTLELSNGVIVKINNQLTDSNTKYFHKLNIPKLD ^F SSQADLR	Human (2821-2880)
KFIEGKLDTVASLQTEKNMVEFNNGMIVKINNPIILDSHTKYFHKLSIPRLD ^F SSKASFN	Hamster (frag 1)
K ^A IEGKSDTVASLHTEKNEVEFNNGMTVKVNNQLTDSHTKYFHKLSVPRLD ^F SSKASLN	Mouse (frag 1)
NEIKTLLKAGHIAWTSSGKGSWKWACPRFSDEGTHESQISFTIEG ^L PLTSFGLSNKINSKH	Human (2881-2940)
NEIKMLLEAGHVAVWTSSGTGSWNWACPNFSDEGTHSSKISFTVEGPIAFFGLSNNINGKH	Hamster (frag 1)
NEIKTLLLEAGHVALTSSGTGSWNWACPNFSDEGIHSSQISFTVDGPIAFVGLSNNINGKH	Mouse (frag 1)
LRVNQNLVYESGSLNFSKLEIQSQVDSQHVGH ^S VL TAKGMALFGE ^G KAFTGRHDAHLNG	Human (2941-3000)
L ^R VIQKLAYESGFLNYSML ^E SVESKVESQHV ^G SSILTGKGTVLLREAKAEMTGEHNADLNG	Hamster (frag 1)
L ^R VIQKLTYESGFLNYSKFEVESKVESQHV ^G SSILTANGRALLKDAKAEMTGEHNANLNG	Mouse (frag 1)
KVIGTLKNSLFFSAQPFEITASTNNEGNLKVRFPLRLTGKIDFLNNYALFLSPSAQQASW	Human (3001-3060)
KVIGTLKNSLFFSAQPFMITASTNNDGNLKV ^S FP ^L KL TGKIDFLNNYALFLSPHAQQASW	Hamster (frag 1)
KVIGTLKNSLFFSAQPFEITASTNNEGNLKVGFPLKL TGKIDFLNNYALFLSPRAQQASW	Mouse (frag 1)

FIG. 14B1

ALIGNMENT OF HUMAN 2701-3540 SEQ ID NO:214 WITH HAMSTER SEQ ID NO:215 AND MOUSE SEQ. ID
 NO:216 APOB-100 SEQUENCES

LNDFQVPDLHIPEFQLPHISHTIEVPTFGKLYSILKIQSPLFTLDANADIGNGTTSANEA-	Human (2701-2760)
EFQLPRLSHTIEIPAFGR ^L LHGILKIQSPLFILDANANIQNVTTLENKAE	Hamster (frag 1)
EFQLPHLSHTIEIPAFGKL ^H SILKIQSPLFILDANANIQNVTTSGNKAE	Mouse (frag 1)
GIAASITAKGESKLEVLNFDFAQNAQLSNPKINPLALKESVKFSSKYLRT ^E HGSEM ^L FFG	Human (2761-2820)
IVASIAAT-GESEIEALNFDFAQAQFLELNP ^N PLILKESMNFSSKHARMEHEGEILFSG	Hamster (frag 1)
IVAS-VTAKGESQFEALNFDFAQAQFLELNP ^H PPVLKESMNFSSKHVRMEHEGEIVFDG	Mouse (frag 1)
NAIEGKSNTVASLHTEKNTLELSNGVIVKINNQLTDSNTKYFHKLNI ^P KLDFSSQADLR	Human (2821-2880)
KFIEGKLDTVASLQTEKNMVEFNNGMIVKINNPIILDSHTKYFHKL ^S IPRLDFSSKASFN	Hamster (frag 1)
KAIEGKSOTVASLHTEKNEVEFNNGMTVKVNNQLTDSHTKYFHKL ^S VPRLDFSSKASLN	Mouse (frag 1)
NEIKTL ^L KAGHIAWTSSGKGSKWACPRFSDEGTHESQISFTIEG ^L PLTSFGLSNKINSKH	Human (2881-2940)
NEIKMLLEAGHVAVTSSGTGSWNWACPNFSD ^E GTHSSKISFTVEGP ^I AFFGLSNNINGKH	Hamster (frag 1)
NEIKTLLEAGHVALTSSGTGSWNWACPNFSD ^E GIHSSQISFTVDGP ^I AFVGLSNNINGKH	Mouse (frag 1)
LRVNQNLVYESGSLNFSKLEIQSQVDSQHVGH ^S VL TAKGMALFGE ^G KAFTGRHDAHLNG	Human (2941-3000)
LRVIQKLAYESGFLNYSMLEVESKVESQHV ^G SSIL TGKGTVLLREAKAEMTGEHNADLNG	Hamster (frag 1)
LRVIQKL ^T YESGFLNYSKFEVESKVESQHV ^G SSILTANGRALLKDAKAEMTGEHNANLNG	Mouse (frag 1)
KVIGTLKNSLFFSAQPFEITASTNNEG ^N LKVRFP ^L RLTGKIDFLNNYALFLSPSAQQASW	Human (3001-3060)
KVIGTLKNSLFSFAQP ^F MITASTNNDGNLKV ^S FP ^L KL ^T KGKIDFLNNYALFLSPHAQQASW	Hamster (frag 1)
KVIGTLKNSLFFSAQPFEITASTNNEG ^N LKV ^G FP ^L KL ^T KGKIDFLNNYALFLSPRAQQASW	Mouse (frag 1)

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FIG. 14B2

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ALIGNMENT OF HUMAN 2701-3540 SEQ ID NO:214 WITH HAMSTER SEQ ID NO:215 AND MOUSE SEQ. ID
 NO:216 APOB-100 SEQUENCES

QVSARFNQYKYNQNF	SAGNNENIMEAHV	GINGEANLDFLNI	PLTIPEMRLPY	TIITPPL	Human (3061-3120)
QVSARFNQYKYNQNF	SAINNEH	IEAHVGM	DANLDFLTI	PLTIPEVKLPYIGL	TPPL Hamster (frag 1)
QASTRFNQYKYNQNF	SAINNEH	IEASIGM	DANLDFLNI	PLTIPEINLPYTEFK	TPPL Mouse (frag 1)
KDFSLWEKTGLKEFL	KTTKQSF	DLSVKAQYKKN	KHRHSITN	PLAVLCEFISQSIKS	FDRH Human (3121-3180)
KDFSWEETGLK----	KQSF	DLSVKAQYKKN	RDRHSIAI	PLNGFYEFILNNV	DGIGK Hamster (frag 1)
KDFSWEETGLKEFL	KTTKQSF	DLSVKAQYKKN	SDKHSIVV	PLGMFYEFILNNV	NSWDRK Mouse (frag 1)
FEKRNNALDFVTKSY	NETKIKFDKY	KAESQDEL	PRTFQIPGY	TVPVVNV	VEVSPFTIEM Human (3181-3240)
IGKVRDSALDYLISS	YNEAKNKFEN----	SLIQ	SRTFQKRGY	TIPFVNIEV	TPFTVET Hamster (frag 1)
FEKVRNNALHFLTTSY	NEAKIKVDKY	KTENSLNQ	PSGTQFNHGY	TIPVNVIEV	SPFAVET Mouse (frag 1)
SAFGYVFPKAVSMPS	FILGSDVR	VPSTLILPS	LELPVLHV	PRNL-KLSLPH	FKELCTIS Human (3241-3300)
LASSHVIPK	AINTPSVHIL	GNVIVPSYRLV	PSLELPVLRV	PRNLLKFSLP	PDFKELRTID Hamster (frag 1)
LASRHV	IP	TAISTPSVTIP	GNIMVPSYKLVLP	PLELPVFHGP	NLFKFFLPDFKGFNTID Mouse (frag 1)
HIFIPAMGNITYDFS	FKSSVITLNT	NAELFNQSDI	VAHLLSSSS	VIDALQYKLEG	TTRL Human (3301-3360)
NIYIPALGNFTYDFS	FKSSVITLNT	NVGLYNRSDI	VAHFLSSSS	FVTDALQYKLEG	TSRL Hamster (frag 1)
NIYIPAMGNFTYDFS	FKSSVITLNT	NAGLYNQSDI	VAHFLSSSS	FVTDALQYKLEG	TSRL Mouse (frag 1)
TRKRGLKLATALSL	SNKFVEGSH	NSTVSLTTKN	MEVSVAKTT	KAEI--PILRMN	FKQELNGN Human (3361-3420)
TRKRGLKLATADSL	TNKFVKGN	HDSTFSLTKKN	MEASV-KTT-ANL	HAPILTMNF	FKQELNGN Hamster (frag 1)
MRKRGLKLATAVSL	TNKFVKGS	HDSTISLTKKN	MEASV-RTT-ANL	HAPIFSMN	FKQELNGN Mouse (frag 1)

FIG. 14B3

ALIGNMENT OF HUMAN 2701-3540 SEQ ID NO:214 WITH HAMSTER SEQ ID NO:215 AND MOUSE SEQ. ID
 NO:216 APOB-100 SEQUENCES

TKSKPTVSSMEFKYDFNSSMLYSTAKGAVDHLKLSLESLTSYFSIESSTKGDVKGSVLSR	Human (3421-3480)
AKSKPIVSSSIELNYDFNSSKLYSTAKGGVDHKKFSLESLTSYFSIESSTKGNIKGSVLSQ	Hamster (frag 1)
TKSKPTVSSSIELNYDFNSSKLSHSTATGGIDHKKFSLESLTSYFSIESFTKGNIKSSFLSQ	Mouse (frag 1)
EYSGTIASEANTYLNKSTRSSVKLQGTSKIDDIWNLEVKENFAGEATLQRIYSLWEHST	Human (3481-3540)
EYSGSVASEANTYLN	Hamster (frag 1)
EYSGSVANEANVYLN	Mouse (frag 1)

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FIG. 14B3 Cont.

ALIGNMENT OF HUMAN 3481-4536 SEQ ID NO:217 WITH RAT SEQ ID NO:218 APOB-100 SEQUENCES

EYSGTIASEANTYLN <u>SKSTRSSVK</u> LQGT <u>SKIDDIWN</u> LEVKENFAGEATLQRIYSLWEHST	Human (3481-3540)
NSKGRSSVRLQASNFAGIWNFEVGENFAGEATLRRYYGTWEHNM	Rat (frag 2)
KNHLQLEGLFFTNGEHTSKATLELSPWQMSALVQVHASQPSSFHDFPDLGQEQVALNANTK	Human (3541-3600)
INHLQVFSYFDTKGQTCRATLELSPWTMSTLLQVHVSPSPFLDLHHFDQDEVILKASTK	Rat (frag 2)
NQKIRWKNEVRIHSGSFQSQVELSNDQEKAHLDIAGSLEGHLRFLKNIILPVYDKSLWDF	Human (3601-3660)
NQKVSWKSEVQVESQVLQHNAHFSNDQEEVRLDIAGSLEG-----QLWDL	Rat (frag 2)
-----	Human
ENFFLPAFGKS-----	Rat (frag 2)
LKLDVTTSIGRRQHLRVSTAFVYTKNPNGYSFIPVKVLADKFITPGLKNDLNSVLVMP	Human (3661-3720)
LR-ELLQIDGKROYLQASTSLHYTKNPNGYLLSLPVQELTDRFIIPGLKLNDF-----	Rat (frag 2)
TFHVPFTDLQVPSCKLDFREIQIYKKLRTSSFALNPLTLPEVKFPEVDVLTKYSQPEDSL	Human (3721-3780)
-----SGIKIYKKLSTSPFALNLTMLPKVKFPGVDLLTQYSKPEGSS	Rat (frag 2)
IPFFEITVPESQLTVSRFTLPKSVSDGIAALDNAVANKIADFELPTIIVPEQTIEIPSI	Human (3781-3840)
VPTFETTIPEIQLTVSQFTLPKSFVPVGNTVFDLNKLTNLIADVDLPSITLPEQTIEIPSL	Rat (frag 2)
KFSVPAGIVIPSFQALTARFEVDSPPVYNATWSASLKNKADYVETVLDSTCSSTVQFLEYE	Human (3841-3900)
EFSPAGIFIPFFGELTAHVGMASPLYNVTWSTGWKNKADHVETFLDSTCSSTLQFLEYA	Rat (frag 2)

FIG. 14C1

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Alignment of Human 3481-4536 SEQ ID NO:217 with Rat SEQ ID NO:218 apoB-100
 Sequences

LNLVGLTHKIEDGTLASKTKGTLAHRDFAEYEEDGKFEGLEQWEGKAHLNIKSPAFTDLH	Human (3901-3960)
LKVVGTHRIENDKFIYKIKGTLQHCDNFVNKYNEDGIFEGLDLEGEAHLDITSPALTDHF	Rat (frag 2)
LRYQDKKIGISTSAASPAVGTGMDDEDDDFSKWNFYSPQSSPDKKLTIFKTELVRVE	Human (3961-4020)
LHYKEDKTSVSASASPAGTIVSLDASTDDQSVRLHVYFRPQSPDNKLSIFKMEWRDKE	Rat (frag 2)
SDEETQIKVNWEEEAASGLLTSLKDNVPKATGVLVDYVVKYHWEHTGLTLREVSSKLRN	Human (4021-4080)
SDGETYIKINWEEEAARLLDSLKSNVPKASEAVDYVKKYHLGH-----ASSELRKS	Rat (frag 2)
LQNNAEWVYQGAIRQIDIDVRFQKAASGTTGTYQEWKDKAQLYQELLTOEQQASFOGL	Human (4081-4140)
LQNDAEH---AIRMVDEMNVNAQRVTRDTYQSL-YKKMLAQE-----SQSIPEKL	Rat (frag 2)
KDNVFDGLVRVTQKFHMKVKHLIDSLIDFLNFRFPQFGPKGIYTREELCTMFIREVGTV	Human (4141-4200)
KKMVLGSLVRITQKYHMAVTWLMDSVIHFLKFNRVQFPGNAGTYTVDELYTIAMRETKKL	Rat (frag 2)
LSQVYSKVHNGSEILFSYFQDLVITLPELRLKHKLIDVISMYRELLKDLKEAQEVFKAI	Human (4201-4260)
LSQLF----NGLGHLFSYVQDQV-----EKSRVINDI-----TFKCPFSP	Rat (frag 2)
QSLKTTEVLRLNLQDLLQFIFQLIEDNIKQKEMKFTYLINYIQDEINTIFNDYIPYVFKL	Human (4261-4320)
TPCKLKDVLLIFREDNLILSNLGQQDINFTTILSDQSFLERLDIIIEKIEC-LKNN--	Rat (frag 2)
-----	Human
ESTCVPDHINMFFKTHIPFAFKS-----	Rat (frag 2)

FIG. 14C1 Cont.

Alignment of Human 3481-4536 SEQ ID NO:217 with Rat SEQ ID NO:218 apoB-100
 Sequences

LKENLCLNLHKFNEFIQNELQEASQELQQIHQYIMALREEYFDPSIVGWTVKYYEELEEKI	Human (4321-4380)
LRENIYSVFSEFNDVQSILQEGSYKLQQVHQYMKAFREEYFDPSVVGWTVKYYEIEEKM	Rat (frag 2)
VSLIKNLLVALKDFHSEYIVSASNFTSQLSSQVEQFLHRNIQEYLSILTDPDGKGKEKIA	Human (4381-4440)
VDLIKTLAPLRDFYSEYSVTAADFASKMSTQVEQFVSRDIREYLSMLADINGKGRKVA	Rat (frag 2)
ELSATAQEIIKSQAIATKKIISDYHQQFRYKQLQDFSDQLSDYYEKFAESKRLIDLSIQN	Human (4441-4500)
ELSIVVKERIKSWSTAVAEITSDYLRQLHKLQDFSDQLSGYYEKFAESTRLIDLSIQN	Rat (frag 2)
YHTFLIYITELLKKLQSTTMN--PYMKLAPGELTIIL	Human (4501-4536)
YHMFRLRYIAELLKKLQVATANNVSPYLRFQAQGELIITF	Rat (frag 2)

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FIG. 14C2

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Alignment of Human 4141-4536 SEQ ID NO:219 with Chicken SEQ ID NO:220 apoB-100 Sequences

KDNVFDGLVRVTQKFHMVKHLIDSLIDFLNFRFPQFGKPGIYTRRELCTMFIREVGTV	Human (4141-4200)
IPGLSEKYTGEEPLYMTTEKAAKT	Chicken (frag 1)
LSQVYSKVHNGSEILFSYFQDLVITLPFELRKHKLIDVISMYRELLKDLSKEAQEVFKAI	Human (4201-4260)
ADICLSKLQEYFDALIAAISELEVRVPASETILRGRNVLDQIKEMLKHLQEKIRQTFVTL	Chicken (frag 1)
QSLKTTEVLRLNQDLLQFIFQLIEDNIKQLKEMKFTYLINYIQDEINTIFNDYIPYVFKL	Human (4261-4320)
QEADFAGKLNRLKQVVQKTFQKAGNMVRSLSQKNFEDIKVMQQLYKDAMASDYAHKLRS	Chicken (frag 1)
LKENCLNLHKFNEFIQNELQEASQELQQIHQYIMALREEYFDPSIVGWTVKYYEELEEKI	Human (4321-4380)
LAENVVKYISQIKNFSQKTLQKLSENLQQLVLYIKALREEYFDPTTLGWSVKYYEVEDKV	Chicken (frag 1)
VSLIKNLLVALKDFHSEYIVSASNFTSQLSSQVEQLHRNIQEYLSILTPDGKGKEKIA	Human (4381-4440)
LGLLKNLMDTLVIWYNEYAKDLSDLVTRLTDQVRELVENYRQEYYDLITDVEGKGRQKVM	Chicken (frag 1)
ELSATAQEIIKSQAIAATKKIISDYHQQFRYKQLQDFSDDLSDYYEKFIAESKRLIDLSIQN	Human (4441-4500)
ELSSAAQEKIRYWSAVAKRKINEHNRQVKAKLQEIYGQLSDSQEKLINVAKMLIDLTV EK	Chicken (frag 1)
YHTFLIYITELLKKLQSTTMNPMYKLAGELTIIL-----	Human (4501-4536)
YSTFMKYIFELLRWFEQATADSIKPYIAVREGELRIDVPFDWEYINQMPQKSREALRNKV	Chicken (frag 1)
-----	Human
ELTRALIQQGVEQGRKWEEMQAFIDEQLATEQLSFQQIVENIQKRMKT	Chicken (frag 1)

FIG. 14D

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Alignment of Human 1561-1740 SEQ ID NO:221 with Rabbit SEQ ID NO:222 apoB-100

Sequences

DMTFSKQNALLRSEYQADYESLRFFSLLSGSLNSHGLELNADILGTDKINSGAHKATLRI	Human (1561-1620)
DLTFSKQNALLRAEYQADYKSLRFFFTLLSGLLNTHGLELNADILGTDKMMNTAAHKATLRI	Rabbit (frag 1)
GQDGI STATTNLKCSLLVLENELNAELGLSGSMKLT TNGRFREHNAKFSLDGKAALTE	Human (1621-1680)
GQNGVSTATTSLRYSPLMLENELNAELALSGSMKLTATNGRFKEHNAKFSLDGKATLTE	Rabbit (frag 1)
LSLGSAYQAMILGVDSKNIFNFKVSQEGKL SNDMMGSAEMKFDHTNSLNIAGLSLDFS	Human (1681-1740)
LSLGSAYQAMILGADSKNIFNF-----	Rabbit (frag 1)

FIG. 14E

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Alignment of Human 3301-3720 SEQ ID NO:223 with Rabbit SEQ ID NO:224 apoB-100
 Sequences

HIFIPAMGNITYDFSKSSVITLNTNAELFNQSDIVAHLLSSSSVIDALQYKLEGTTRL-	Human (3301-3360)
MASEKGPSNKDYT	Rabbit (frag 2)
TRKRGKLATALSLSNKFVEGSHNSTVSLTTKNMEVSVAKTTKAEIPILRMNFKQELNGN	Human (3361-3420)
LRRRI-----EPWEFEVFFDPQELRKEACLLYEIKWGASSKTWRSSGKNNTTNH-VEVN	Rabbit (frag 2)
-----	Human
FLEKLT	Rabbit (frag 2)
TKSKPTVSSSMEFKYDFNSSMLYSTAKGAVDHKLSLESLSYFSIESSTKGDVKGSVLSR	Human (3421-3480)
-----	Rabbit (frag 2)
EYSGTIASEANTYLNKSTRSSVKLQGTSKIDDIWNLEVKENFAGEATLQRIYSLWEHST	Human (3481-3540)
RKEACLLYEIKWGASSKTWRSSGK-NTTNHVEVNF-LE-KLTSEGRLGPSTCCSI-----	Rabbit (frag 2)
KNHLQLEGLFFTNGEHTSKATLELSPWQMSALVQVHASQPSFFHDFPDLGQEVALNANTK	Human (3541-3600)
TWFLSWS--PCWECSMAIREFLSQHPGVTLIIIFVARLFQHMDRNRQGLKDLVTSQVTVR	Rabbit (frag 2)
NQKIRWKNEVRIHSGSFQSQVELSNDQEKAHLDIAGSLEGLRFLKNIILPVYDKSLWDF	Human (3601-3660)
VMSVSEYCYCWENFVNYPGKAAQWPRYPWRMLMYALELYCIILGLPPC-----	Rabbit (frag 2)
LKLDVTTSIGRRQHLRVSTAFVYTKNPNGYSFIPVKVLADKFITPGLKNDLNSVLVMP	Human (3661-3720)
-----LKISRRHQKQL-----TFFSLTPQYCHYKMIPPYILLATGLLQPSVPWR	Rabbit (frag 2)

FIG. 14F

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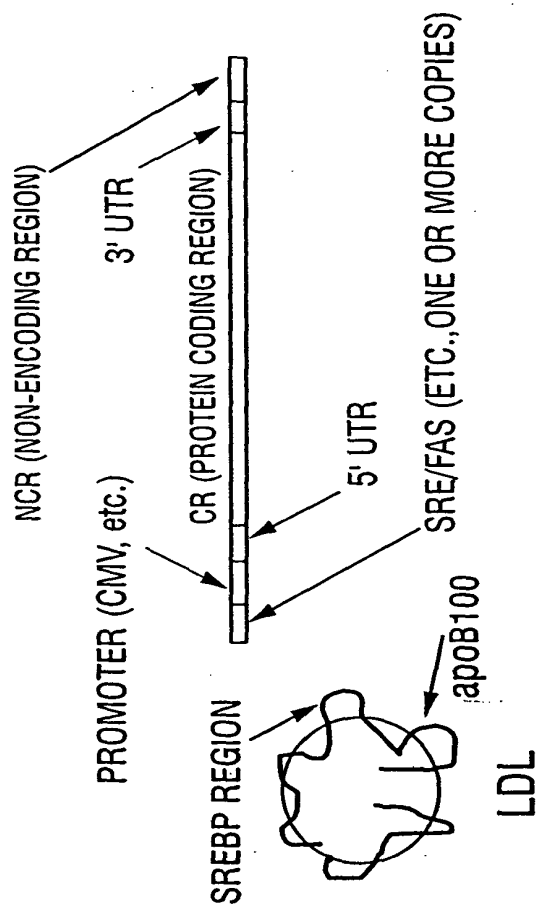


FIG. 15